PUBLIC HEALTH RISK ASSESSMENT
881 HILLSIDE AREA (OU1)
TECHNICAL MEMORANDUM NO. 9
TOXICITY CONSTANTS

Department of Energy
Rocky Flats Plant
Golden, Colorado

ENVIRONMENTAL RESTORATION PROGRAM
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EXECUTIVE SUMMARY

This technical memorandum summarizes the relevant toxicity constants for the 22 contaminants of concern (COCs) identified for the Public Health Evaluation (PHE) of the Baseline Risk Assessment (BRA) for Operable Unit No. 1 (OU1) in the 881 Hillside area at the Rocky Flats Plant (RFP). It does not include the Environmental Evaluation (EE) portion of the BRA. Toxicity constants will be used in the risk assessment to evaluate potential adverse effects from exposure to site-related chemicals. Toxicological data from the U.S. Environmental Protection Agency (EPA 1992a,b; 1991) were evaluated to determine the severity of toxic properties associated with the COCs. In this Technical Memorandum, chronic values are presented, since a goal of the PHE is to determine whether long-term exposure to site-related COCs is expected to cause adverse effects in exposed individuals. Chronic effects are a better measure of long-term impacts than acute effects.

COCs were classified into two groups, carcinogens and noncarcinogens, because health risks are calculated differently for these agents. Certain contaminants may have both properties (e.g., 1,1,-dichloroethene and carbon tetrachloride). Potential effects from chronic exposure to noncarcinogenic compounds will be assessed by comparing exposure levels to chronic reference doses (RfDs). Unlike carcinogenic compounds, substances that cause systemic toxicity (i.e., toxic effects other than cancer) appear to do so through mechanisms that include a physiological threshold. A certain dose of a compound (i.e., the RfD dose) must therefore be present before exposed individuals may experience toxic effects. Conversely, potential carcinogenic effects are expressed as the probability (using chemical-specific cancer slope factors, or SFs) that an individual will develop cancer from a lifetime exposure. Cancer SFs for nonradiological compounds represent the 95th percentile confidence limit on the probability of a carcinogenic response, while SFs for radionuclides are best estimates (i.e., median or 50th percentile values).

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LIST OF ACRONYMS AND ABBREVIATIONS

BaP	Benzo(a)pyrene
BRA	Baseline Risk Assessment
COC	Contaminants of Concern
EE	Environmental Evaluation
ECAO	Environmental Criteria Assessment Office
EPA	Environmental Protection Agency
ITEF	International Toxicity Equivalency Factor
IAG	Interagency Agreement
IRIS	Integrated Risk Information System
LOAEL	Lowest Observed Adverse Effect Level
MF	Modifying Factor
mg/kg-d	milligrams per kilogram per day
NOAEL	No Observed Adverse Effect Level
OU1	Operable Unit 1
PAH	Polycyclic Aromatic Hydrocarbons
PHE	Public Health Evaluation
RAGS	Risk Assessment Guidance for Superfund
RCRA	Resource Conservation and Recovery Act
RfD	Reference Dose
RFI/RI	RCRA Facility Investigation/Remedial Investigation
RFP	Rocky Flats Plant
RPM	Remedial Project Manager
SF	Slope Factor
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
UF	Uncertainty Factor

1.0 INTRODUCTION

1.1 Purpose

The purpose of this technical memorandum is to present the toxicity constants that will be used in the Public Health Evaluation (PHE) of the Baseline Risk Assessment (BRA) for Operable Unit No. 1 (OU1) in the 881 Hillside area located at the Rocky Flats Plant (RFP), as specified in Attachment 2, Section VII.D of the Interagency Agreement (IAG 1991). These toxicity constants will be integrated with calculated daily intakes in the risk characterization portion of the PHE to yield quantitative risk estimates. This memorandum is being submitted prior to submittal of the BRA for OU1 as specified in Attachment 2, Section VII.D of the IAG.

1.2 Scope

The scope of this Technical Memorandum is limited to identifying human toxicity constants for the OU1 contaminants of concern (COCs) identified in *Technical Memorandum No. 8, Contaminant Identification* (DOE 1992). The 22 COCs are identified in Table 1-1. The toxicity constants include reference doses (RfDs) for noncarcinogens and their associated uncertainty factors (UFs) and cancer slope factors (SFs) and weight-of-evidence classifications for carcinogens. Since reference concentrations are not available for the contaminants of concern, noncarcinogenic toxicity will be evaluated based on reference doses. The parameter distributions under development at Oak Ridge National Laboratory are beyond the scope of this technical memorandum and will be presented in the draft PHE. Toxicological profiles for each COC will be presented in the PHE portion of the Phase III RFI/RI Report.

TABLE 1-1

CONTAMINANTS OF CONCERN MATRIX FOR OU1 BY MEDIA

Contaminant	Ground Water	Surface Soil	Surface Water	Sediment
1,1-Dichloroethene	X			
total 1,2-Dichloroethene	X			
1,1,1-Trichloroethane	X			
Acenaphthene		X		X
Americium-241		X	X	X
AROCLOR-1254		X		X
Benzo(a)anthracene		X		X
Benzo(a)pyrene		X		X
Benzo(b)fluoranthene		X		X
Benzo(k)fluoranthene		X		X
Carbon Tetrachloride	X			
Chloroform	X			
Dibenzo(a,h)anthracene		X		X
Dichlorodifluoromethane	X			
Fluoranthene		X		X
Fluorene		X		X
Methylene Chloride	X			
Plutonium-239,-240		X	X	X
Pyrene		X		X
Tetrachloroethene	X			
Trichloroethene	X			
Trichlorofluoromethane	X			

2.0 TOXICITY CONSTANTS FOR OU1

Toxicity assessment evaluates the nature and extent of health effects from exposure to site-related chemicals. It consists of a hazard identification and a dose-response evaluation. The hazard identification involves a comprehensive review of toxicity data to identify the severity of toxic properties associated with the COCs. Once the potential toxicity of a chemical has been established, the next step is to determine the amount of chemical exposure that may result in adverse human health effects (i.e., to establish the dose-response relationship for each COC). Thus, the toxicity assessment evaluates the increased likelihood of adverse health effects as a result of human exposure to site-related contaminants.

OU1 COCs were classified into two broad groups, carcinogens and noncarcinogens, because health risks are calculated differently for these agents. Certain contaminants (e.g., 1,1-dichloroethene and carbon tetrachloride) can have both properties.

The toxicity constants were developed according to the steps presented in the Risk Assessment Guidance for Superfund (RAGS) (EPA 1989). The U.S. Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) and *Health Effects Assessment Summary Tables* (EPA 1992 a,b; 1991) were the primary sources of information. Secondary sources of information include: EPA Region IV guidance (EPA 1992c) and Environmental Criteria Assessment Office (ECAO).

2.1 Toxicity Constants for Noncarcinogens

An RfD embodies EPA's principal approach and rationale for assessing health effects other than cancer. Unlike carcinogenic agents, substances that cause systemic toxicity (i.e., toxic effects other than cancer) do so through mechanisms that include a physiological threshold. Thus, a certain dose of a compound must be present before noncarcinogenic toxic effects will be observed. This approach assumes that there is some level of exposure (i.e., the RfD value) that individuals can tolerate without experiencing adverse, systemic

health effects. Conversely, if exposure exceeds this threshold, there may be some concern that exposed individuals will experience noncarcinogenic health effects.

In general, the RfD is an estimate (with an established UF) of a daily exposure to the human population, including sensitive subpopulations, likely to be without appreciable risk of deleterious effects over a lifetime. RfDs are calculated by dividing a NOAEL (No Observed Adverse Effect Level) or a LOAEL (Lowest Observed Adverse Effect Level) dose in milligrams per kilograms per day (mg/kg-day) obtained from human or animal studies by an UF. UFs are used to ensure health protective standards for all segments of a potentially affected population. Each UF generally consists of multiples of ten, with each factor representing a specific area of uncertainty inherent in the extrapolation from the available data. The bases for applying different UFs are explained below:

- If the NOAEL is based on human data, an UF of 10 is usually applied to account for variation in sensitivities among individuals. It is intended to protect sensitive subpopulations (e.g., the elderly and children).
- If the NOAEL is based on animal data, an additional UF of 10 is used to account for the interspecies variability between humans and other animals.
- If the NOAEL is derived from a subchronic instead of a chronic study, an additional UF of 10 is applied to extrapolate a subchronic value to a chronic value.
- If a LOAEL is used instead of a NOAEL, an additional UF of 10 is used to account for the uncertainty associated with extrapolating from LOAELs to NOAELs.

Modifying factors (MFs) may also be applied. MFs range from 1 to 10 and reflect uncertainties not specifically addressed by the above-mentioned UFs. In general, RfDs represent an estimate of the potential toxicity of a chemical and with variability typically spanning one order of magnitude (EPA 1992b). Table 2-1 lists the RfDs and the associated UFs for OU1 noncarcinogens that are currently available from EPA. Inhalation RfDs for 1,1-dichloroethene, chloroform, and trichloroethene are pending in IRIS (EPA 1992a). The

oral RfD for 1,1,1-trichloroethene has been withdrawn from IRIS (EPA 1992a), while oral RfDs for 1,2-cis-dichloroethene and trichloroethene are pending.

TABLE 2-1

NONCARCINOGENIC TOXICITY CONSTANTS

Chemical	Chronic Oral RfD (mg/kg-d)	Uncertainty Factor	Chronic Inhalation RfD (mg/kg-d)	Uncertainty Factor
1,1-Dichloroethene	9×10^{-3}	1,000	P	ND
1,1,1-Trichloroethane	W	ND	ND	ND
1,2-cis-dichloroethene	P	ND	ND	ND
1,2-trans-dichloroethene	2×10^{-2}	1,000	ND	ND
Acenapthene	0.06	3,000	ND	ND
Carbon tetrachloride	7×10^{-4}	1,000	ND	ND
Chloroform	0.01	1,000	P	ND
Dichlorodifluoromethane	0.2	100	ND	ND
Fluoranthene	0.04	3,000	ND	ND
Fluorene	0.04	3,000	ND	ND
Methylene chloride	0.06	100	ND	ND
Pyrene	0.03	3,000	ND	ND
Tetrachloroethene	1×10^{-2}	1,000	ND	ND
Trichloroethene	P	ND	P	ND
Trichlorofluoromethane	0.3	1,000	ND	ND

ND = An inhalation RfD and its associated uncertainty factor for that compound have not yet been determined.
W = Oral RfD has been withdrawn from IRIS (EPA 1992a).
P = An RfD is pending in IRIS (EPA 1992a).
Sources: IRIS (EPA 1992a), EPA (1991), EPA (1992b).

2.2 Toxicity Constants for Carcinogens

Numerical estimates of potency for potential carcinogens are presented as cancer SFs. Cancer SFs and the estimated chronic daily intake of a compound, averaged over a lifetime of exposure, are used to estimate the incremental risk that an individual exposed to that compound may develop cancer. Evidence of carcinogenicity comes from two sources: lifetime studies with laboratory animals and human studies where excess cancer risk is associated with exposure to a carcinogen. For most carcinogens, animal data from laboratory experiments represent the primary basis for developing toxicity constants. If a carcinogenic response occurs at the exposure level used in the studies, it is assumed that a similar response will occur at all lower doses, unless evidence to the contrary exists. Exposure to any level of a chemical carcinogen is therefore assumed to have a finite risk of inducing cancer. This mechanism for carcinogenesis is referred to as stochastic, which means that there is theoretically no level of exposure to this material that does not pose a small, but finite, probability of generating a carcinogenic response.

Since risks at low levels of exposure cannot be quantified directly from either animal or epidemiological studies, mathematical models are typically used to extrapolate from high to low doses. A linearized multistage model for low-dose extrapolation has been promulgated and approved by EPA (1986). Use of this model provides a health-protective, upper-bound (conservative) estimate of risk.

Uncertainty in assessing the carcinogenicity of a chemical is managed by grouping chemicals into one of several groups according to the weight of evidence from epidemiological studies and/or animal studies:

Group A - Human Carcinogen (sufficient evidence of carcinogenicity in humans)

Group B - Probable Human Carcinogen (B1-limited evidence of carcinogenicity in humans; B2-sufficient evidence of carcinogenicity in animals with inadequate or absence of evidence in humans)

Group C - Possible Human Carcinogen (limited evidence of carcinogenicity in animals and inadequate or no human data)

Group D - Not Classifiable as to Human Carcinogenicity (inadequate or no evidence)

Group E - Evidence of Noncarcinogenicity for Humans (no evidence of carcinogenicity in adequate studies)

Carcinogenic COCs for OU1 were divided into two groups: nonradiological carcinogens and radionuclides. These distinctions were made because cancer SFs for radionuclides and nonradionuclides are derived differently (see Sections 2.2.1 and 2.2.2) and have different units $(mg/kg\text{-}day)^{-1}$ versus picocuries $(pCi)^{-1}$. In addition, polycyclic aromatic hydrocarbons (PAHs) have been identified as a subset of nonradionuclides because they are derived using a toxicity weighting scheme based on the measured value of benzo(a)pyrene (BaP).

2.2.1 Toxicity Constants for Nonradiological Carcinogens

Assuming a linear dose-response relationship at low doses of chemical exposure, the SF for nonradiological carcinogens defines the probability that an individual will develop cancer from a lifetime exposure to one unit of carcinogen. Because these SFs represent the 95th percentile confidence limit on the probability of a carcinogenic response, risk estimates are upper-bound values. Thus, there is only a 5 percent probability that the actual risk is greater than the estimated risk. Cancer risk assessment in this context yields upper-bound risk estimates. Individual cancer risk will be calculated as the product of exposure to a chemical (in mg/kg-day) and the SF for that chemical (in $[mg/kg\text{-}day]^{-1}$). Cancer risks from exposure to multiple carcinogens across all exposure pathways will be summed. Table 2-2 lists the toxicity constants that have been determined for nonradiological carcinogens.

TABLE 2-2

TOXICITY CONSTANTS FOR NONRADIOLOGICAL CARCINOGENS

Chemical	Weight of Evidence	Oral Slope Factor $(mg/kg\text{-}day)^{-1}$	Inhalation Slope Factor $(mg/kg\text{-}day)^{-1}$
1,1-Dichloroethene	C[a]	0.6	0.18[b]
AROCLOR-1254[d]	B2	7.7	ND[c]
Carbon tetrachloride	B2	1.3×10^{-1}	0.05[e]
Chloroform	B2	6.1×10^{-3}	0.08[f]
Methylene chloride	B2	7.5×10^{-3}	1.7×10^{-3}[g]
Tetrachloroethene	B2	NA[h]	NA[h]
Trichloroethene	B2	1.1×10^{-2}	W[i]

[a] Inclusion of Group C carcinogens in quantitative risk estimates is done on a case-by-case basis.
[b] Based on the inhalation unit risk factor of 5×10^{-5} $\mu g/m^3$ in IRIS (EPA 1992a).
[c] ND = A slope factor for this compound and pathway has not yet been determined.
[d] Values are for polychlorinated biphenyls.
[e] Based on the inhalation unit risk factor in IRIS (EPA 1992a) of 1.5×10^{-5} $\mu g/m^3$.
[f] Based on the inhalation unit risk factor in IRIS (EPA 1992a) of 2.3×10^{-5} $\mu g/m^3$.
[g] Based on the inhalation unit risk factor in IRIS (EPA 1992a) of 4.7×10^{-7} $\mu g/m^3$.
[h] According to IRIS (EPA 1992a), carcinogenic data are pending.
[i] The SF for that compound has been withdrawn from IRIS (EPA 1992)

Sources: IRIS (EPA 1992a), EPA (1991), EPA (1992b).

The majority of PAHs found in the environment appear to be less toxic than BaP. Exceptions include methylated PAHs and those containing oxygen and nitrogen. Currently, EPA has not specified SFs for PAHs other than BaP. In the past, risk assessors have assumed that all PAHs are equally as toxic as BaP. Recently, risk assessors have proposed using a toxicity equivalency factor (TEF) approach for determining the carcinogenicity of PAHs using BaP as the reference point. EPA's ECAO office recommended that individual

RPMs and Regions use their best judgment when deciding to use a TEF approach for risk assessments involving PAHs. Cancer SFs for PAHs of concern were derived using the TEF approach adopted by EPA Region IV (February 1992) (Table 2-3). SFs derived for the five PAHs of concern for OU1 are shown in Table 2-3.

TABLE 2-3

TOXICITY CONSTANTS FOR POLYCYCLIC AROMATIC HYDROCARBONS

PAH	TEF[a]	Oral Slope Factor[b] $(mg/g\text{-}day)^{-1}$	Inhalation Slope Factor $(mg/kg\text{-}day)^{-1}$
Benzo(a)pyrene	1.0	5.8	NA
Benzo(a)anthracene	0.1	0.58	NA
Benzo(b)fluoranthene	0.1	0.58	NA
Benzo(k)fluoranthene	0.1	0.58	NA
Dibenzo(a,h)anthracene	1.0	5.8	NA

[a] Toxicity Equivalency Factor (TEF) approach adopted by Region IV (February 1992).

[b] Oral slope factors were derived by multiplying the oral slope factor for BaP of 5.8 $(mg/kg\text{-}day)^{-1}$ times the TEF listed in column two for each PAH.

2.2.2 Toxicity Constants for Radionuclides

An extensive body of literature exists that describes the health effects of radionuclides on humans and animals. Intensive research by national and international commissions has resulted in the establishment of universally accepted limits to which workers and the public may be exposed without clinically detectable effects. This literature has resulted in EPA classifying all radionuclides as Group A carcinogens because they emit ionizing radiation, which, at high doses, has been associated with increased cancer incidence in humans. Data derived from both human and animal studies are used by EPA to construct the radionuclide SFs, which are listed in Table 2-4. These non-threshold SFs account for the following: (1) the amount of radionuclide transported into the bloodstream; (2) the decay of radioactive progeny within the body; (3) the distribution and retention of the radionuclide and its

progeny (if any) in the body; (4) the radiation dose delivered to specific organs and tissues; and (5) the age and sex of the exposed individuals (EPA 1992b).

As in the chemical risk models, radiation models extrapolate cancer risks at low doses from risks observed at higher doses using non-threshold, linear dose-response relationships. Because of the radiation risk models employed, SFs for radionuclides are characterized as best estimates (i.e., median or 50th percentile estimates) of the age-averaged lifetime excess cancer risk (fatal and non-fatal) per unit of activity inhaled or ingested.

TABLE 2-4

TOXICITY CONSTANTS FOR RADIONUCLIDES

COC	Weight of Evidence	Oral Slope Factor $(pCi)^{-1}$	Inhalation Slope Factor $(pCi)^{-1}$
Americium - 241	A	2.4×10^{-10}	3.2×10^{-8}
Plutonium - 239, 240	A	2.3×10^{-10}	3.8×10^{-8}

Source: EPA (1992b).

REFERENCES

DOE, 1992. *Public Health Evaluation, 881 Hillside Area (OU1), Draft Technical Memorandum No. 8, Contaminant Identification*, U.S. Department of Energy, Rocky Flats Plant, September 1992.

IAG, 1991. *Rocky Flats Interagency Agreement between the State of Colorado, the Environmental Protection Agency, Environmental Protection Agency, and the Department of Energy*, January 1991.

U.S. Environmental Protection Agency (EPA), 1991. *Health Effects Assessment Summary Tables, Annual FY-1991*, OERR 9200.6-303(91-1), PB91-921199, Office of Emergency and Remedial Response, Washington, DC.

U.S. Environmental Protection Agency (EPA), 1992a. *Integrated Risk Information System*, (IRIS).

U.S. Environmental Protection Agency (EPA), 1992b. *Health Effects Assessment Summary Tables*, OHEA ECOA-CIN-821, Office of Research and Development, Washington, DC.

U.S. Environmental Protection Agency (EPA) Region IV, 1992c. *New Interim Region IV Guidance*, Atlanta, GA.

U.S. Environmental Protection Agency (EPA), 1989. *Risk Assessment Guidance for Superfund, Volume I, Human Health Evaluation Manual (Part A)*, EPA 540/1-89-002, Office of Emergency and Remedial Response, Washington, DC.